AR201-13380A

HIGH PRODUCTION VOLUME (HPV)

CHEMICAL CHALLENGE PROGRAM

ASSESSMENT PLAN

For The

OLEFIN HYDROFORMYLATION PRODUCTS CATEGORY

CAS# 68527-03-7: Pentene, HOF
CAS# 68938-02-3: Pentene, HOF, low-boiling
CAS# 70955-11-2: Hexene, HOF
CAS# 70955-03-2: Hexene, HOF, low-boiling
CAS# 68526-80-7: Alcohols, C6 and C8 iso, distillation residues
CAS# 70955-04-3: Hexene, HOF, high-boiling
CAS# 68527-04-8: Heptene, HOF
CAS# 68526-96-5: Heptene, HOF, low-boiling
CAS# 68526-88-5: Heptene, HOF, high-boiling
CAS# 68527-05-9: Octene, HOF
*CAS# 68938-03-4: Octene, HOF, low-boiling
CAS# 68526-89-6: Octene, HOF, high-boiling
CAS# 68938-04-5: Nonene, HOF
CAS# 68526-93-2: Nonene, HOF, low-boiling
CAS# 68526-90-9: Nonene, HOF, high-boiling
CAS# 68516-18-7: Decene, HOF
CAS# 68527-06-0: Dodecene, HOF
*CAS# 68526-92-1: Dodecene, HOF, low-boiling
CAS# 68526-91-0: Dodecene, HOF, high-boiling

* Not an HPV material, included to facilitate category evaluation.

Prepared by:

ExxonMobil Chemical Company

November 29, 2001

EXECUTIVE SUMMARY

Under the United States Environmental Protection Agency High Production Volume (HPV) Chemical Challenge Program (Program), ExxonMobil Chemical Company has committed to voluntarily compile data for a category of substances defined as olefin hydroformylation products. This category is supported by data for physicochemical, environmental fate and effects, and human health effects endpoints.

ExxonMobil Chemical Company considers the olefin hydroformylation products a category under the HPV Program because their physicochemical and toxicological properties are expected to be very similar and follow a regular pattern as a result of their chemical composition. Products in this category are composed of olefins and alkyl alcohols and are described as "alkyl alcohol bottoms". These products are residual waste materials remaining from the production of alkyl alcohols, which includes the hydroformylation of pentene, hexene, heptene, octene, nonene, decene, and dodecene. Low, intermediate, and high boiling alkyl alcohol bottom products are included in this category, each containing a mixture of hydroformylation reactants (olefins) and finished products (alcohols).

The olefins and alkyl alcohols in the olefin hydroformylation products each have a common structure and incrementally increase in carbon number from the lowest to the highest molecular weight product. The structural similarity of chemicals in each of the two groups creates a predictable pattern in the following parameters: physicochemical properties, environmental fate and effects, and human health effects. Because the olefin hydroformylation products are mixtures of alkyl alcohols and their corresponding olefins, combined data from these groups are used to support this test plan. This plan is based on the assumption that the environmental fate and effects, and human toxicological properties of products in the Olefin Hydroformylation Products Category are equivalent to the combined properties of the olefin and respective alcohol. The data for these two groups of products will come from the Alkyl Alcohols C6 - C13 Category and Higher Olefins Category test plans that have been previously submitted under the HPV Program.

The test data compiled for the category anchor studies is adequate to support a screening-level hazard assessment for the Olefin Hydroformylation Products Category and its member products (CAS numbers 68527-03-7, 68938-02-3, 70955-11-2, 68527-04-8, 68527-05-9, 68938-04-5, 68516-18-7, 68527-06-0, 68938-02-3, 70955-03-2, 68526-80-7, 68526-96-5, 68526-93-2, 70955-04-3, 68526-88-5, 68526-89-6, 68526-90-9, 68526-91-0). Member products that lack measured data for selected HPV endpoints can be characterized by extrapolating or interpolating the existing data associated with the component chemicals. For some endpoints, computer modeled data can be used to further support a hazard assessment.

Evaluation of the olefin hydroformylation products as a category has several advantages:

- The data from this category will be used to inform the public about the potential hazards of olefin hydroformylation products.
- Developing a data matrix of anchor studies and applying justifiable read across practices will provide a sufficiently robust data set to characterize each endpoint in the HPV Program without having to conduct a test for each endpoint and product.
- This resourceful use of existing data will result in fewer animals needed for testing purposes while adequately assessing the potential hazards of products in the Olefin Hydroformylation Products Category.

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TEST PLAN FOR OLEFIN HYDROFORMYLATION PRODUCTS

I. INTRODUCTION

Under the United States Environmental Protection Agency High Production Volume (HPV) Chemical Challenge Program (Program), ExxonMobil Chemical Company has committed to voluntarily compile data for a category of substances defined as olefin hydroformylation products. This category is supported by data for physicochemical, environmental fate and effects, and human health effects endpoints.

ExxonMobil Chemical Company considers the olefin hydroformylation products a category under the HPV Program because their physicochemical and toxicological properties are expected to be very similar and follow a regular pattern as a result of their chemical composition. Products in this category are composed of olefins and alkyl alcohols and are described as "alkyl alcohol bottoms". These products are residual waste materials remaining from the production of alkyl alcohols, which includes the hydroformylation of pentene, hexene, heptene, octene, nonene, decene, and dodecene. Low, intermediate, and high boiling alkyl alcohol bottom products are included in this category, each containing a mixture of hydroformylation reactants (olefins) and finished products (alcohols).

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Evaluation of the Olefin Hydroformylation Products as a category has several advantages:

- The data from this category will be used to inform the public about the potential hazards of the olefin hydroformylation products.
- Developing a data matrix of anchor studies and applying justifiable read across practices will provide a sufficiently robust data set to characterize each endpoint in the HPV Chemical Challenge Program without having to conduct a test for each endpoint and product.
- This resourceful use of existing data will result in fewer animals needed for testing purposes while adequately assessing the potential hazards of products in the Olefin Hydroformylation Products Category.

II. CHEMICAL PROCESS AND DESCRIPTION

Products in the Olefin Hydroformylation Products Category are produced by the hydroformylation of pentene, hexene, heptene, octene, nonene, decene, and dodecene. Hydroformylation refers to the reaction between a branched olefin and a mixture of carbon monoxide and hydrogen to produce an aldehyde, which is then hydrogenated to yield the alcohol. The olefin(s) and associated alcohol(s) by carbon number for the CAS numbers in this category are listed in Table 1.

Exposure to Olefin Hydroformylation Products is generally very low since most of the product is recycled and used in feedstocks. Limited quantities have been sold in the United States and Europe for diesel/fuel oil blending. However, since these products are primarily site-limited intermediates, the potential for exposure is quite low.

Low, intermediate, and high boiling alkyl alcohol bottom products are included in this category, each containing a mixture of hydroformylation reactants (olefins) and finished products (alcohols). Thus, each member of the category is composed of the olefin and corresponding alcohol with an incremental change in carbon number for these components across the category.

The structural similarity of chemicals in each of the two groups creates a predictable pattern in the following parameters: physicochemical properties, environmental fate and effects, and human health effects. The compositional features of members of the category are as follows:

- A mix of olefins and alkyl alcohols.
- An incremental increase in carbon number of the olefin and corresponding alkyl alcohol across category members.

Table 1. CAS Number, Description, and Carbon Number(s) of the Olefin and Corresponding Alcohol for each of the Hydroformylation Products.

CAS Number	Product name	Olefin	Alcohol
68527-03-7	Pentene, HOF	C5	C6
68938-02-3	Pentene, HOF, low-boiling	C5	C6
70955-11-2	Hexene, HOF	C6	C7
70955-03-2	Hexene, HOF, low-boiling	C6	C7

CAS Number	Product name	Olefin	Alcohol
68526-80-7	Alcohols, C6 and C8 iso, distillation residues	-	C6, C8
70955-04-3	Hexene, HOF, high-boiling	-	C7-8
68527-04-8	Heptene, HOF	C7	C8
68526-96-5	Heptene, HOF, low-boiling	C7	C8
68526-88-5	Heptene, HOF, high-boiling	-	C8-9
68527-05-9	Octene, HOF	C8	C9
68938-03-4*	Octene, HOF, low-boiling	C8	C9
68526-89-6	Octene, HOF, high-boiling	-	C9-10
68938-04-5	Nonene, HOF	C9	C10
68526-93-2	Nonene, HOF, low-boiling	C9	C10
68526-90-9	Nonene, HOF, high-boiling	-	C10-11
68516-18-7	Decene, HOF	C10	C11
68527-06-0	Dodecene, HOF	C12	C13
68526-92-1*	Dodecene, HOF, low-boiling	C10-12	C13
68526-91-0	Dodecene, HOF, high-boiling	-	C13-14

* Not an HPV material, included to facilitate category evaluation.

Evaluation of the olefin hydroformylation products as a category accomplishes the goal of the Challenge Program - to obtain screening level hazard information - through the strategic evaluation of data for products within this category. The test plan strategy is based on the principle that:

- These products behave in a similar and/or predictable manner, and
- Interpolation and extrapolation of data can be used to characterize the olefin hydroformylation products for which data are not available.

Procedures to assess the reliability of selected studies described in this test plan are based on the guidelines described by Klimisch *et al.*, 1997.

III. TEST PLAN RATIONALE

A. Physicochemical Data

Physicochemical data (i.e., melting point, boiling point, vapor pressure, water solubility, and Kow) for selected chemical components in the Olefin Hydroformylation Products Category will be calculated using the EPIWIN© model (EPIWIN, 1999), as discussed in the EPA document titled "The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program." These data will be presented as ranges, based on the chemical components selected to represent each olefin hydroformylation product. In addition, measured data for some of these endpoints will also be provided for selected alcohol and olefin components where readily available. Where possible, the measured and calculated data will be presented together for comparative purposes.

Table 2 lists selected measured physicochemical data (boiling range, vapor pressure, and specific gravity) as they appear on the material safety data sheets for products in this category. These data are provided with this test plan to further justify these products as a distinct category under the HPV Program. As shown by the data in Table

2, the structural similarity within each of the two types of chemicals in the olefin hydroformylation products results in a predictable and incremental pattern of physiochemical properties.

Table 2. Selected Physical Properties of Olefin Hydroformylation Products

CAS NUMBER	CHEMICAL NAME	PRIMARY COMPONENTS	BOILING RANGE (° C)	VAPOR PRESSURE (mm Hg @ 100° C)	SPECIFIC GRAVITY	WATER SOLUBILITY (mg/L)*
68527-03-7	Pentene, HOF	**C6 Alcohol**	152-163	124	0.82	10,340-11,950
		C5 Olefin	44-54	506-635	0.65	210-245
68938-02-3	Pentene, HOF, low-boiling	**C6 Alcohol**	152-163	124	0.82	10,340-11,950
		C5 Olefin	44-54	506-635	0.65	210-245
70955-11-2	Hexene, HOF	**C7 Alcohol**	167-176	78	0.83	3,539-11,950
		C6 Olefin	63-73	143	0.69	47-76
70955-03-2	Hexene, HOF, low-boiling	**C7 Alcohol**	167-176	78	0.83	3,539-11,950
		C6 Olefin	63-73	143	0.69	47-76
68526-80-7	Alcohols, C6 and C8 iso, distillation residues	**C6,C8 Alcohol**	152-193	27-124	0.82-0.83	1,379-11,950
		-	-	-	-	-
70955-04-3	Hexene, HOF, high-boiling	**C7-C8 Alcohol**	167-193	27-78	0.83	1,379-11,950
		-	-	-	-	-
68527-04-8	Heptene, HOF	**C8 Alcohol**	185-193	27	0.83	1,379-1,485
		C7 Olefin	85-100	45	0.72	16.9-33.8
68526-96-5	Heptene, HOF, low-boiling	**C8 Alcohol**	185-193	27	0.83	1,379-1,485
		C7 Olefin	85-100	45	0.72	16.9-33.8
68526-88-5	Heptene, HOF, high-boiling	**C8-C9 Alcohol**	185-215	16-27	0.83-0.84	164-1,485
		-	-	-	-	-
68527-05-9	Octene, HOF	**C9 Alcohol**	203-215	16	0.84	164-614
		C8 Olefin	110-116	30	0.73	1.0-5.9
68938-03-4	Octene, HOF, low-boiling	**C9 Alcohol**	203-215	16	0.84	164-614
		C8 Olefin	110-116	30	0.73	1.0-5.9
68526-89-6	Octene, HOF, high-boiling	**C9-C10 Alcohol**	203-224	8.2-16	0.84	75.0**-614
		-	-	-	-	-
68938-04-5	Nonene, HOF	**C10 Alcohol**	217-224	8.2	0.84	75.0**
		C9 Olefin	135-146	5.2	0.74	0.7-1.5
68526-93-2	Nonene, HOF, low-boiling	**C10 Alcohol**	217-224	8.2	0.84	75.0**
		C9 Olefin	135-146	5.2	0.74	0.7-1.5
68526-90-9	Nonene, HOF, high-boiling	**C10-C11 Alcohol**	217-241	3.8-8.2	0.84	28.0-75.0
		-	-	-	-	-
68516-18-7	Decene, HOF	**C11 Alcohol**	229-241	3.8	0.84	28.0**
		C10 Olefin	163-172	1.6	0.74	1.0
68527-06-0	Dodecene, HOF	**C13 Alcohol**	256-266	2.7	0.84	5.8**
		C12 Olefin	204-214	0.2	0.76	0.1
68526-92-1	Dodecene, HOF, low-boiling	**C13 Alcohol**	256-266	2.7	0.84	5.8**
		C10-C12 Olefin	163-214	0.2-1.6	0.74-0.76	0.1-1.0
68526-91-0	Dodecene, HOF, high-boiling	**C13-C14 Alcohol**	275-310***	0.3***	0.84***	0.8***
		-	-	-	-	-

* Calculated using EPIWIN
** Measured values (Robust summaries are attached)
*** Read across values from a C13-C15 alcohol

B. Human Health Effects

The structural and compositional similarity of the olefin hydroformylation products influences both their physicochemical (Table 2) and their toxicological properties (Table 4). Since olefin hydroformylation products are mixtures of alkyl alcohols and higher olefins, their toxicity can be assessed by evaluating the existing data on alkyl alcohols and higher olefins. As a chemical category, the olefin hydroformylation products, have predictable, low-level environmental and health hazards.

ExxonMobil Chemical Company believes the category of olefin hydroformylation products is scientifically justifiable and that the test data compiled for the category proves adequate to support a screening-level hazard assessment for the category and its members (CAS numbers 68527-03-7, 68938-02-3, 70955-11-2, 68527-04-8, 68527-05-9, 68938-04-5, 68516-18-7, 68527-06-0, 68938-02-3, 70955-03-2, 68526-80-7, 68526-96-5, 68526-93-2, 70955-04-3, 68526-88-5, 68526-89-6, 68526-90-9, 68526-91-0). One can assess the untested endpoints by interpolation between and among the category members.

The alcohol component of the olefin hydroformylation products would likely be broken down by mitochondrial beta-oxidation or by cytochrome P450 mediated omega and omega-minus-one oxidation (may be followed by beta-oxidation). The alcohol undergoes various oxidative steps to yield other alcohols, ketones, aldehydes, carboxylic acids and carbon dioxide (Mann, 1987). Data for monohydric, aliphatic alcohols show a systematic variation according to molecular weight in a manner similar to many other homologous series (Monick, 1968). The body handles aliphatic hydrocarbons in a similar manner via oxidative conversion to alcohols, ketones, and eventual elimination as carbon dioxide and carboxylic acids (Wislocki et al, 1980). The undegraded alcohols can be conjugated either directly or as a metabolite with glucuronic acid, sulfuric acid, or glycine and are rapidly excreted (Lington and Bevan, 1994). Intermediate aldehydes could be reactive and bind with DNA and/or proteins. Glucuronidation and glutathione conjugation are possible means of rapid elimination (Mann, 1987).

Table 3 summarizes the data available for the components of each product and the read across strategy applied to the data gaps. Table 4 summarizes the available data used to characterize the toxicity of the olefin hydroformylation products.

Table 3. Olefin Hydroformylation Products Data Matrix For Mammalian Toxicity Studies

Olefin Hydroformylation Product		Component		Acute Toxicity	Genotox. Point Mutation	Genotox. Chrom. Aberr.	Subchronic Toxicity**	Developmental Toxicity**
CAS #	Product name	Alcohol	Olefin	Oral	Ames	M. Micron.		
68527-03-7	Pentene, HOF	C6	C5	A	RA	RA	A	A
68938-02-3	Pentene, HOF, low-boiling	C6	C5	A	RA	RA	A	A
70955-11-2	Hexene, HOF	C7	C6	A	O	O	RA	T(O)
70955-03-2	Hexene, HOF, low-boiling	C7	C6	A	O	O	RA	T(O)
68526-80-7	Alcohols, C6 and C8 iso, distillation residues	C6, C8	-	A	A	A	A	A
70955-04-3	Hexene, HOF, high-boiling	C7-C8	-	A	RA	RA	A	A
68527-04-8	Heptene, HOF	C8	C7	A,O*	A	A,O	A	A
68526-96-5	Heptene, HOF, low-boiling	C8	C7	A,O*	A	A,O	A	A
68526-88-5	Heptene, HOF, high-boiling	C8-C9	-	A	A	A	A	A
68527-05-9	Octene, HOF	C9	C8	A,O	RA	RA	A	A
68938-03-4	Octene, HOF, low-boiling	C9	C8	A,O	RA	RA	A	A
68526-89-6	Octene, HOF, high-boiling	C9-C10	-	A	RA	RA	A	A
68938-04-5	Nonene, HOF	C10	C9	H,A,O	O	O	RA	A
68526-93-2	Nonene, HOF, low-boiling	C10	C9	H,A,O	O	O	RA	A
68526-90-9	Nonene, HOF, high-boiling	C10-C11	-	H,A	RA	RA	A	A
68516-18-7	Decene, HOF	C11	C10	H,A	RA	RA	A	A
68527-06-0	Dodecene, HOF	C13	C12	A,O	A	RA	A	RA
68526-92-1	Dodecene, HOF, low-boiling	C13	C10-C12	A,O	A	RA	A	T(O)
68526-91-0	Dodecene, HOF, high-boiling	C13-C14	-	A	A	RA	A	RA

A: Data comes from the corresponding alcohol; Studies are reliable (Robust Summaries presented).
O: Data comes from the corresponding olefin; Studies are reliable (Robust Summaries presented).
H: Data is on the hydroformylation mixture; Studies are reliable (Robust Summaries presented).
RA Read Across Extrapolation. T(O): Testing proposed in ACC Higher Olefins Test Plan. O*: Acute dermal data.
** Reproductive toxicity will be assessed by read-across to Developmental Toxicity Studies and Repeat Dose Toxicity Studies that included histopathology on male and female sex organs and accessory sex organs.

Table 4. Summary of Toxicology Data for Olefin Hydroformylation Products

Olefin Hydroformylation Product		Acute Toxicity	Genotox. Point Mutation	Genotox. Chrom. Aberr.	Subchronic Toxicity** NOAEL	Developmental Toxicity** NOAEL
CAS #	Product name	Oral (Dermal)	Ames	M. Micron.		
68527-03-7	Pentene, HOF					
	C6Alcohol	3.7 g/kg (>2.6 g/kg)	RA	RA	=0.5% in diet (rat, dog) = 2.0 mg/kg/day (rat, dermal)	Inhal: Dam/Pup = 3500 mg/m^3
	C5 Olefin	RA	RA	RA	RA	RA
68938-02-3	Pentene, HOF, low-boiling					
	C6Alcohol	3.7 g/kg (>2.6 g/kg)	RA	RA	=0.5% in diet (rat, dog) = 2.0 mg/kg/day (rat, dermal)	Inhal: Dam/Pup = 3500 mg/m^3
	C5 Olefin	RA	RA	RA	RA	RA
70955-11-2	Hexene, HOF					
	C7 Alcohol	=3.9 g/kg (> 3.2 g/kg)	RA	RA	RA	RA
	C6 Olefin	RA	Negative	Negative	RA	T (C6 Olefin)
70955-03-2	Hexene, HOF, low-boiling					
	C7 Alcohol	=3.9 g/kg (> 3.2 g/kg)	RA	RA	RA	RA
	C6 Olefin	RA	Negative	Negative	RA	T (C6 Olefin)
68526-80-7	Alcohols, C6 and C8 iso, distillation residues					
	C6, C8 Alcohol	3.7 g/kg (>2.6 g/kg)	Negative (2-ethyl-1-hexanol)	Negative (2-ethyl-1-hexanol)	=0.5% in diet (rat, dog) = 2.0 mg/kg/day (rat, dermal)	Inhal: Dam/Pup = 3500 mg/m^3
	-	-	-	-	-	-
70955-04-3	Hexene, HOF, high-boiling					
	C7-C8 Alcohol	=3.9 g/kg (> 3.2 g/kg)	RA	RA	= 2.0 mg/kg/day (rat, dermal) =130 mg/kg/day (rat) NOEL = 125 mg/kg/day (LOEL = 250 mg/kg/day) (rat)	Dam: 500 mg/kg/day Pup: 1000 mg/kg/day Inhal: Dam/Pup 400 mg/m^3
	-	-	-	-	-	-

Table 4. Continued

Olefin Hydroformylation Product		Acute Toxicity	Genotox Point Mutations	Genotox Chrom. Aber.	Subchronic Toxicity** NOAEL	Developmental Toxicity** NOAEL
68527-04-8	Heptene, HOF					
	C8 alcohol	> 2.0 g/kg (> 2.6 g//kg)	Negative (2-ethyl-1-hexanol)	Negative (2-ethyl-1-hexanol)	= 2.0 mg/kg/day (rat, dermal) =130 mg/kg/day (rat) NOEL = 125 mg/kg/day (LOEL = 250 mg/kg/day) (rat)	Dam: 500 mg/kg/day Pup: 1000 mg/kg/day Inhal: Dam/Pup 400 mg/m^3
	C7 Olefin	RA (> 3.2 g/kg)	RA	Negative	RA	RA
68526-96-5	Heptene, HOF, low-boiling					
	C8 Alcohol	> 2.0 g/kg (> 2.6 g//kg)	Negative (2-ethyl-1-hexanol)	Negative (2-ethyl-1-hexanol)	= 2.0 mg/kg/day (rat, dermal) =130 mg/kg/day (rat) NOEL = 125 mg/kg/day (LOEL = 250 mg/kg/day) (rat)	Dam: 500 mg/kg/day Pup: 1000 mg/kg/day Inhal: Dam/Pup 400 mg/m^3
	C7 Olefin	RA (> 3.2 g/kg)	RA	Negative	RA	RA
68526-88-5	Heptene, HOF, high-boiling					
	C8-C9 Alcohol	> 2.0 g/kg (> 2.6 g//kg)	Negative (2-ethyl-1-hexanol)	Negative (2-ethyl-1-hexanol)	=130 mg/kg/day	Dam: 500 mg/kg/day Pup: 1000 mg/kg/day Inhal: Dam/Pup 400 mg/m^3
	-	-	-	-	-	-
68527-05-9	Octene, HOF					
	C9 Alcohol	= 3.0 g/kg (> 3.2 g/kg)	RA	RA	= 144 mg/kg/day	Dam: 144 mg/kg/day Pup: 144 mg/kg/day
	C8 Olefin	> 5.0 g/kg (> 3.2 g/kg)	RA	RA	RA	RA
68938-03-4	Octene, HOF, low-boiling					
	C9 Alcohol	= 3.0 g/kg (> 3.2 g/kg)	RA	RA	= 144 mg/kg/day	Dam: 144 mg/kg/day Pup: 144 mg/kg/day
	C8 Olefin	> 5.0 g/kg (> 3.2 g/kg)	RA	RA	RA	RA
68526-89-6	Octene, HOF, high-boiling					
	C9-C10 Alcohol	= 3.0 g/kg (> 3.2 g/kg)	RA	RA	= 144 mg/kg/day	Dam: 158 mg/kg/day Pup: 790 mg/kg/day
	-	-	-	-	-	-

Table 4. Continued

Olefin Hydroformylation Product		Acute Toxicity	Genotox. Point Mutation	Genotox. Chrom. Aber.	Subchronic Toxicity** NOAEL	Developmental Toxicity** NOAEL
68938-04-5	Nonene, HOF	> 5.0 g/kg (> 3.2 g/kg)				
	C10 Alcohol	= 4.6 g/kg	RA	RA	RA	Dam: 158 mg/kg/day Pup: 790 mg/kg/day
	C9 Olefin	> 2.3 g/kg (> 2.3 g/kg)	Negative	Negative	RA	RA
68526-93-2	Nonene, HOF, low-boiling	> 5.0 g/kg (> 3.2 g/kg)				
	C10 Alcohol	= 4.6 g/kg	RA	RA	RA	Dam: 158 mg/kg/day Pup: 790 mg/kg/day
	C9 Olefin	> 2.3 g/kg (> 2.3 g/kg)	Negative	Negative	RA	RA
68526-90-9	Nonene, HOF, high-boiling	> 5.0 g/kg (> 3.2 g/kg)				
	C10-C11 Alcohol	= 4.6 g/kg (> 2.6 g/kg)	RA	RA	100 mg/kg/day	Dam: 158 mg/kg/day Pup: 790 mg/kg/day
	-	-	-	-	-	-
68516-18-7	Decene, HOF	> 5.0 g/kg (> 3.2 g/kg)				
	C11 Alcohol	= 4.6 g/kg (> 2.6 g/kg)	RA	RA	100 mg/kg/day	Dam/Pup: > 1,440 mg/kg/day
	C10 Olefin	RA	RA	RA	RA	RA
68527-06-0	Dodecene, HOF					
	C13 Alcohol	> 2.0 g/kg	Negative (1-dodecanol)	RA	= 100 mg/kg/day	RA
	C12 Olefin	> 7.7 g/kg (> 2.5 g/kg)	RA	RA	RA	RA
68526-92-1	Dodecene, HOF, low-boiling					
	C13 Alcohol	> 2.0 g/kg	Negative (1-dodecanol)	RA	= 100 mg/kg/day	RA
	C10-C12 Olefin	> 7.7 g/kg (> 2.5 g/kg)	RA	RA	RA	T (C18 Olefin)
68526-91-0	Dodecene, HOF, high-boiling					
	C13-C14 Alcohol	> 2.0 g/kg	Negative (1-dodecanol)	RA	= 100 mg/kg/day	RA
	-	-	-	-	-	-

RA Read Across Extrapolation.

** Reproductive toxicity will be assessed by read-across to Developmental Toxicity Studies and Repeat Dose Toxicity studies that included histopathology on male and female sex organs and accessory sex organs.

T: Test proposed in ACC Higher Olefins test plan.

C. Presentation of Olefin Hydroformylation Products Category Data Associated with the Anchor Studies under the HPV Challenge Program

Acute Oral Toxicity

All of the olefin hydroformylation products have a low order of toxicity to rats via the oral route of exposure based on data from the hydroformylation products themselves as well as data from the corresponding alkyl alcohols and higher olefins (Table 4). The LD_{50} for the hydroformylation products is greater than 5.0 g/kg. The LD_{50} for the C6 branched and linear alkyl alcohol anchor study was >3.7 g/kg (Scala, 1973). The LD_{50}'s for the C6-C8, C7-C9, C8-C10, C9-C11, and C11-C14 branched alkyl alcohols were all > 2 g/kg. For all of the alkyl alcohols, acute oral exposure induced signs of systemic toxicity that were characterized by depression, sedation, and ataxia. These results demonstrate that members of the alkyl alcohol category have a consistent, low order of acute oral toxicity. The higher olefins also have a low order of acute toxicity. For all of the higher olefins, the LD_{50} was at least greater than 2.3 g/kg. Taken together, the acute toxicity data for the alkyl alcohols and the higher olefins demonstrates that the olefin hydroformylation products have a low order of acute toxicity.

Acute Dermal Toxicity

The Olefin hydroformylation products have a low order of toxicity via the dermal route of exposure based on data from the hydroformylation products themselves as well as the component alkyl alcohols and olefins (Table 4). The dermal LD_{50} for all of the hydroformylation products was greater than 3.2 g/kg. The rabbit dermal LD_{50} for all of the alkyl alcohols was greater than 2.6 g/kg. This indicates that the members of this category have a consistent pattern of acute toxicity via the dermal route of exposure.

Genotoxicity

In Vitro:
Based on mutagenicity data for alkyl alcohols and higher olefins, Olefin hydroformylation products are not considered mutagenic (Table 4). The weight of evidence from this existing data supports the conclusion that these materials are not genotoxic and obviates the need for further testing.

Mutagenicity data on alcohol components:
Existing data on 1-hexanol, which is an isomer of Alkyl Alcohol C6, indicates that this material is not genotoxic. Although a robust summary for this study is not provided, the summary is available in IUCLID (ECBa). In addition, 2-ethyl-1-hexanol and 1-dodecanol were evaluated in Ames assays in the presence and absence of metabolic activation. The 2-ethyl-1-hexanol is an isomer of Alkyl Alcohol C7-C9, and the 1-dodecanol is an isomer of Alkyl Alcohol C11-C14. Both materials were not mutagenic in Ames assays using five strains of *Salmonella typhimurium.*

Additional data to support the assessment of mutagenicity comes from the alkyl acetates, which are metabolized to the corresponding alkyl alcohol. The members of this category have been extensively evaluated for mutagenicity and have been shown to

be non-mutagenic (EMCCa). For further details on the assessment of the mutagenicity of alkyl alcohols, please refer to the EMCC Test Plan for Alkyl Alcohols (EMCCb).

Mutagenicity data on higher olefin components:
Higher olefins have been evaluated for mutagenicity in Ames assays. Both C_6 and C_9 olefins were evaluated in Ames assays in the presence and absence of metabolic activation. Both materials produced negative results, indicating that they are not mutagenic. In addition, bacterial mutagenicity studies on larger molecular weight higher olefins, i.e. C20-24 higher olefins, indicate that the higher molecular weight olefins are also not mutagenic. Robust summaries for these studies are available through the ACC Higher Olefins Test Plan (ACC, 2001).

All together, the weight of evidence demonstrates that olefin hydroformylation products are not mutagenic as shown by the negative mutagenicity data on the alcohols and higher olefins.

In Vivo
Based on existing data for alkyl alcohols, higher olefins, and structurally similar materials, members of the Olefin Hydroformylation Products Category are not considered to be clastogenic (Table 4). Existing data in addition to data forthcoming from the Alkyl Alcohols Testing Program will be used to evaluate the clastogenicity of the olefin hydroformylation products.

Clastogenicity data on the alcohols:
A detailed assessment of the clastogenicity of the alkyl alcohols and the proposed testing is presented in the EMCC Test Plan for Alkyl Alcohols (EMCCb) that has been submitted to the US EPA. The assessment is based on existing data for structural isomers of the alkyl alcohols, existing data on metabolic precursors, and forthcoming data on proposed testing for the category. In short, the existing data for structural isomers comes from mouse micronucleus studies on 2-ethyl-1-hexanol (ECBc) and 1-dodecanol (ECBb) and mouse lymphoma studies on 2-ethyl-1-hexanol. The alkyl acetates, as mentioned above, are metabolic precursors to the alkyl alcohols and produced negative results in mouse micronucleus assays (EMCCa). Together, these data demonstrate a consistent pattern of toxicity for the alkyl alcohols and obviates the need for extensive clastogenicity testing of these materials. To complete the category evaluation of the alkyl alcohols, a mouse micronucleus test on the C_6 alkyl alcohol (CAS # 68526-79-4) has been proposed. The results of this test will be compared with the data already available to evaluate the clastogenicity of alkyl alcohols. The forthcoming data from this testing program will be used to complete the assessment of the clastogenicity of olefin hydroformylation products. This strategy will also address animal welfare concerns by reducing the number of animals required to evaluate the category.

Clastogenicity data on higher olefins:
In addition to the negative clastogenicity data for alcohols, studies conducted on higher olefins also indicate that these materials are not clastogenic. Both a C6 and a C9 higher olefin have been evaluated in Ames studies with 5 strains of *Salmonella typhimurium* in the presence and absence of metabolic activation. The results of these tests were negative. These materials as well as a C7 higher olefin were also evaluated

for their ability to induce chromosome aberrations in a mouse micronucleus assay. The C6 higher olefin produced a weakly positive response at the highest dose (5 g/kg) when administered by oral gavage. However, when the material was evaluated in the mouse micronucleus assay following inhalation exposure, the most relevant route of exposure, it produced negative results. Given that the C6 higher olefin was not genotoxic in the Ames test or in the micronucleus test when administered by inhalation and given the very slight response seen in the oral micronucleus assay, the C6 higher olefin is not considered to be genotoxic.

Two other higher olefins, the C7 and C9 olefins also produced negative results in the mouse micronucleus assay. In addition, data from *in vitro* cytogenicity and mouse micronucleus tests on larger molecular weight higher olefins, i.e. C20-24 higher olefins, indicate that the higher molecular weight olefins are also not clastogenic. Robust summaries for these studies are available through the ACC Higher Olefins Test Plan (ACC, 2001). Hence, the weight of evidence shows that the higher olefins are not clastogenic.

In summary, olefin hydroformylation products are not considered clastogenic based on existing data for the alcohols and higher olefins. Additional data produced in the EMCC Alkyl Alcohols testing program can be used to provide further support for this category assessment. Importantly, this strategy will reduce the amount of unnecessary animal testing.

Subchronic Toxicity

As with the previous endpoints, the subchronic toxicity of olefin hydroformylation products will be assessed from the data on alkyl alcohols and higher olefins (Table 4).

Subchronic toxicity data on alcohols:
An evaluation of the repeated dose studies for alkyl alcohols indicates that olefin hydroformylation products have a low order of subchronic toxicity.

A 14-week oral subchronic study was conducted in rats with C11-C14 branched alkyl alcohols at doses of 0, 100, 500, and 1000 mg/kg/day of body weight administered by gavage. At the mid and high-dose levels, females did not display any differences in body weight or food consumption, but had significantly higher mean platelet counts compared to controls. In contrast, males had significantly lower body weights and food consumption, however, hematological parameters were within normal ranges. At the middle and high doses, males and females had significantly higher liver weights than animals in the control group. In addition, males of the high dose group had higher relative brain and testes weights relative to the controls while relative adrenal weight was increased in the high dose females. There were no pathological findings in these tissues, and the organ weight changes were most likely either adaptive responses or merely a consequence of the body weight effects. No other treatment-related weight or histopathological changes were observed in the other organs, including female reproductive organs. The significance of these subtle changes on hematological parameters is unknown, but like the organ weight differences, occurred only after repeat

administration of extremely high doses of Alkyl Alcohols C11-C14 by oral gavage. The NOAEL of this study was 100 mg/kg/day.

Subchronic toxicity data on 1-hexanol, an isomer of Alkyl Alcohol C6, indicates that this material has a low order of subchronic toxicity. Thirteen-week dietary feeding studies in both the rat and dog produced a NOAEL greater than or equal to 0.5% in the diet. Furthermore, a number of studies have evaluated the toxicity of repeated exposure to 2-ethylhexanol, an isomer of Alkyl Alcohol C7-9. In a 3-month study in rats, 2-ethylhexanol was administered by oral gavage at doses of 25, 125, 250, and 500 mg/kg/day. At the highest doses (250 and 500 mg/kd/day), changes in body and organ weights were observed. The NOEL for the study was 125 mg/kg/day and the LOEL for the study was 250 mg/kg/day based on body weight changes. Summaries of the subchronic studies on 1-hexanol and 2-ethylhexanol are publicly available from the European Chemicals Bureau (ECB) IUCLID database and are included with this submission (ECB, 2000).

A 14-day oral study was conducted in Wistar rats with iso-octanol and isononanol at doses of 130 mg/kg/day and 144 mg/kg/day, respectively. Plasma cholesterol and triglycerides were analyzed, the testes and liver were weighed, and the liver was analyzed for both histopathological lesions and the activity of peroxisomal enzymes. No treatment-related effects were observed during the study. Neither iso-octanol nor isononanol induced any significant changes in testes or liver weight, vacuolation, or activity of the peroxisome-associated enzymes. The NOAEL for iso-octanol was the limit dose of 130 mg/kg/day and the NOAEL for isononanol was the limit dose of 144 mg/kg/day.

Dermal exposure of rats to 0.4 and 2.0 mg/kg/day hexyl alcohol or Alkyl alcohol C7 - 9, branched for 10 days resulted in no clinical signs of toxicity at any time during the study. All animals survived to study termination and there were no treatment-related clinical, in-life, gross postmortem or microscopic findings. The no observable adverse effect level (NOAEL) for repeat dermal exposure was 2.0 mg/kg/day.

Taken together, the results of these studies demonstrate that Alkyl Alcohols C6-C13 have a low order or toxicity under conditions of repeat exposure by both the oral and dermal routes. In addition, they demonstrate that the members of the category display a consistent degree of subchronic toxicity by either the oral or dermal routes of exposure. Given that olefin hydroformylation products are composed of alkyl alcohols, these data indicate that they have a low order of subchronic toxicity.

Subchronic toxicity data on higher olefins:
Currently, there are no data to assess the subchronic toxicity of the lower molecular weight higher olefins. However, subchronic toxicity data on a C6 higher olefin is forthcoming through the ACC Higher Olefins Panel (ACC, 2001). In the spirit of reducing unnecessary animal testing and because higher olefins are a component of Olefin Hydroformylation Products, the data from this testing program will support an assessment of the Olefin Hydroformylation Products.

Data from subchronic tests of a higher molecular weight olefin, i.e. C20-24, indicate that these materials have a low order of toxicity in 13-week studies (NOAEL = 1000 mg/kg/day). A robust summary of this data is available through the ACC Higher Olefins Test Plan (ACC, 2001). This data and the forthcoming test data for the C6 olefin will be used to evaluate the subchronic toxicity of the Olefin Hydroformylation Products. Therefore, no subchronic toxicity testing is proposed for the olefin hydroformylation products, as this would be redundant. Furthermore, existing data on the alkyl alcohols demonstrate that olefin hydroformylation products have a low order of toxicity under conditions of repeat exposure by both the oral and dermal routes. In addition, they demonstrate that the members of the category display a consistent degree of subchronic toxicity by either the oral or dermal routes of exposure. Therefore, olefin hydroformylation products do not require further testing to assess subchronic toxicity.

Developmental Toxicity

Studies on the developmental toxicity of the alkyl alcohol and higher olefin components of the olefin hydroformylation products indicate that these materials have a lower order of toxicity and are not considered selective developmental toxicants by either the oral or inhalation routes of exposure (Table 4).

Developmental toxicity studies on alcohols:

Oral Exposure

Studies on the developmental toxicity of Alkyl Alcohols C6-C13 indicate that these materials have a low order of toxicity and are not considered selective developmental toxicants by either the oral or inhalation routes of exposure. Alkyl alcohol C7-9, branched was orally administered at 100, 500, and 1000 mg/kg on gestation days 6-15 in a developmental toxicity study in rats. Maternal toxicity was seen in the high dose group as indicated by emaciation, rales, and hypoactivity. However, no adverse maternal effects were observed in the low or mid-dose groups. In addition, there were no significant signs of fetal toxicity in any of the dose groups. A maternal NOAEL of 500 mg/kg and a fetal NOAEL of 1000 mg/kg were observed.

In another study, the developmental toxicity of isononylalcohol 1 and isononylalcohol 2 were evaluated in Wistar rats. Isononylalcohol 1 consists of isomers with a moderate degree of branching (dimethyl heptanols) and contains approximately 16% isodecanol. Isononylalcohol 2 consists of isomers with a low degree of branching (dimethyl heptanols and methyl octanols). Each test substance was administered by oral gavage at 144, 720, or 1440 mg/kg/day during days 6-15 of gestation. At the middle and high dose levels of isononylalcohol 1, signs of maternal and fetal toxicity, including decreased body weight, were observed. At the lowest dose of isononylalcohol 1, no maternal toxicity was observed. There were an increased number of fetuses with hydroureter. However, the significance of this endpoint as an indicator of marginal developmental toxicity is questionable. Therefore, isononylalcohol 1 was considered to induce developmental toxicity only at doses that induce overt maternal toxicity. Isononylalcohol 2 also produced maternal and fetal effects at both the middle and high doses. At the lowest dose however, no maternal or fetal toxicity was observed.

Therefore, isononylalcohol 2 induced fetal toxicity at doses that also induce overt maternal toxicity. The maternal NOAEL for isononylalcohol 1 and isononylalcohol 2 is 144 mg/kg. The fetal NOAEL for isononylalcohol 1 is less than 144 mg/kg, whereas the fetal NOAEL for isononylalcohol 2 is 144 mg/kg.

In a similar study, the developmental toxicity of isodecanol (isomers of trimethyl heptanols and dimethyl octanols) was evaluated in Wistar rats by oral gavage at doses of 158, 790, and 1580 mg/kg during days 6-15 of gestation. Signs of compound-induced toxicity including reduced body weight were observed in dams of the middle and high dose groups. No maternal signs of toxicity were observed in the low dose group. Fetotoxic effects including reduced mean fetal body weight and skeletal retardations were observed only in the highest dose group. The maternal NOAEL for this study was 158 mg/kg and the fetal NOAEL was 790 mg/kg. Thus, isodecanol is fetotoxic only at doses that produce overt maternal toxicity.

An identical study conducted concurrently on C-7-9-11 alcohol (consists of isomers of heptanol, nonanol, and undecanol) produced negative results at all three dose levels tested: 144, 720, and 1440 mg/kg/day. No adverse effects were observed in dams or in the fetuses at any of these doses. The NOAEL for this study was therefore 1440 mg/kg/day.

Inhalation Exposure

The developmental toxicity resulting from inhalation of saturated vapors has also been evaluated for several members of the Alkyl Alcohols C6 - C13 category. Inhalation of Alkyl Alcohols C6-C13 is the primary concern during industrial use, particularly for the lower molecular weight members of the category. Therefore, an evaluation of inhalation studies is useful for evaluating the developmental toxicity of the category.

The available developmental toxicity data for structural isomers of the Alkyl Alcohols indicate that these materials are not developmentally toxic via the inhalation route of exposure. Inhalation of saturated vapors of 1-hexanol (3500 mg/m^3) resulted in no significant signs of maternal or fetal toxicity. The NOAEL for both maternal and fetal effects for this study was the limit dose of 3500 mg/m^3.

Another study evaluated the developmental toxicity of three structurally related alcohols, 1-octanol, 1-nonanol, and 1-decanol following inhalation. Sprague-Dawley rats were exposed to saturated vapors of 1-octanol (400 mg/m^3), 1-nonanol (150 mg/m^3), and 1-decanol (100 mg/m^3) for 7 hours per day during days 1-19 of gestation. No significant effects, including no changes in maternal weight gain, feed consumption, or water intake were observed between the control and any of the treated groups. In addition, no fetal toxicity was observed, as indicated by fetal body weight, sex ratio, and the number of resorptions. The NOAEL for both maternal and fetal effects for each test substance was the saturated vapor concentration: 1-octanol (400 mg/m^3, 1-nonanol (150 mg/m^3), and 1-decanol (100 mg/m^3).

Collectively, the weight of evidence demonstrates that Alkyl Alcohols C6-C13 have a low order or maternal toxicity and do not induce signs of developmental toxicity until maternal toxicity is observed. Hence, these materials are not selective developmental

toxicants. In addition, the maternal and fetal NOAELs for oral exposure to different members of the category are consistent. Furthermore, the NOAELs for inhalation reflect the maximum achievable vapor concentration. Since these materials are not selective toxicants and display a consistent, low order of developmental toxicity they will not undergo further testing for developmental toxicity.

Collectively, the weight of evidence for alkyl alcohols demonstrates that olefin hydroformylation products have a low order or maternal toxicity and do not induce signs of developmental toxicity until maternal toxicity is observed. Hence, these materials are not selective developmental toxicants. In addition, the maternal and fetal NOAELs for oral exposure to different members of the category are consistent, indicating that there are no major differences in the potency of the category members. The NOAELs for developmental toxicity from inhalation reflect the maximum achievable vapor concentration of each test substance. However, in all cases, the NOAEL exceeded the maximum achievable vapor concentration. Since these materials are not selective toxicants and display a consistent, low order of developmental toxicity they will not undergo further testing for developmental toxicity.

Developmental toxicity of higher olefins:

Developmental studies on the higher olefins, which are also components of the olefin hydroformylation products, are in progress with the ACC Higher Olefins Panel. A developmental/reproductive/subchronic toxicity screen will be conducted on a C6 olefin and a developmental/reproductive screen will be conducted on a C18 olefin. The data and robust summaries of these tests will be forthcoming under the ACC Higher Olefins test plan.

As discussed above, the existing data for the alcohol component of olefin hydroformylation products demonstrates a consistent pattern of toxicity for the category. The forthcoming data under the ACC Higher Olefins Test Program will provide further support to assess developmental toxicity. By taking this approach, the Olefin Hydroformylation Products Category can be evaluated while the generation of redundant data and unnecessary animal testing is minimized.

Reproductive Toxicity

The available developmental toxicity studies and repeat-dose studies prove adequate to support a screening-level hazard assessment for the reproductive toxicity potential of olefin hydroformylation products (Table 4). Developmental toxicity studies conducted by the oral route of exposure on corresponding alkyl alcohols including Isooctyl alcohol, Isononyl alcohol, Isodecanol, and Undecyl alcohol, produced consistent results and demonstrated that these materials do not affect reproductive parameters. Although a slight increase in resorptions was observed in several studies, this only occurred in the highest dose group and in the presence of overt maternal toxicity. Furthermore, inhalation exposure to saturated vapors of 1-hexanol, 1-octanol, 1-nonanol, and 1-decanol did not induce any significant changes in reproductive parameters. In the subacute studies of isooctyl alcohol and isononyl alcohol, no changes in testicular weight were observed. In addition, no histopathological effects in male and female

reproductive organs were observed in the subchronic study conducted on C11-C14 alcohols. These data support the conclusion that the Alkyl Alcohols C6-C13 are not selective reproductive toxicants.

Additional support to evaluate the reproductive toxicity of olefin hydroformylation products is forthcoming from the reproductive toxicity studies proposed in the ACC Higher Olefins Category Test Plan (ACC). To evaluate the reproductive toxicity of the olefin components, a developmental/reproductive/subchronic toxicity screen will be conducted on a C6 olefin and a developmental/reproductive screen will be conducted on a C18 olefin. The data and robust summaries of these tests will be forthcoming under the ACC Higher Olefins test plan.

According to the OECD SIDS Guidelines, adequate developmental toxicology data coupled with subchronic toxicity data that shows no effects on reproductive organs fulfills the requirement for an assessment of reproductive toxicity potential.

D. Aquatic Toxicity

Aquatic endpoints for the HPV Program include acute toxicity to a freshwater fish and invertebrate, and toxicity to a freshwater alga. The olefin and alkyl alcohol components of products in this category have been shown to produce an expected increasing level of toxicity to freshwater organisms with increasing molecular weight of the product components. This is based on data from the literature that are used to read across to selected components of products in this test plan, data specifically for components of the products in this category, as well as on results of computer modeling using ECOSAR (1999) for selected component chemicals [ECOSAR is an aquatic toxicity modeling program and is a subroutine contained in EPIWIN (1999)].

Table 5 identifies the type of data available for the components of each product and the read across strategy applied to the data gaps. Table 6 summarizes the available data used to characterize the aquatic toxicity of olefin hydroformylation products.

Modeled data consistently correlated well with the experimental data used to characterize acute toxicity for the alcohol and olefin components in this category. This suggests that the ECOSAR model is sufficiently robust to accurately calculate the toxicity of this range of chemicals and can be used to develop reliable toxicity data to complete data gaps.

Table 5. Olefin Hydroformylation Products Data Matrix for Aquatic Toxicity, Identifying the Type of Data Available for the Components of each Product and the Read Across Strategy Applied to the Data Gaps

Olefin Hydroformylation Product		Component		Fish Acute Toxicity	Invertebrate Acute Toxicity	Alga Toxicity
CAS #	Product Name	Alcohol	Olefin			
68527-03-7	Pentene, HOF	C6	C5	A, E	E	E
68938-02-3	Pentene, HOF, low-boiling	C6	C5	A, E	E	E
70955-11-2	Hexene, HOF	C7	C6	A, O	A, E	E
70955-03-2	Hexene, HOF, low-boiling	C7	C6	A, O	A, E	E
68526-80-7	Alcohols, C6 and C8 iso, distillation residues	C6, C8	-	A	A	E
70955-04-3	Hexene, HOF, high-boiling	C7-C8	-	RA	RA	RA
68527-04-8	Heptene, HOF	C8	C7	A, E	A, E	E
68526-96-5	Heptene, HOF, low-boiling	C8	C7	A, E	A, E	E
68526-88-5	Heptene, HOF, high-boiling	C8-C9	-	RA	RA	RA
68527-05-9	Octene, HOF	C9	C8	A, O	A, E	A, E
68938-03-4	Octene, HOF, low-boiling	C9	C8	A, O	A, E	A, E
68526-89-6	Octene, HOF, high-boiling	C9-C10	-	RA	RA	RA
68938-04-5	Nonene, HOF	C10	C9	A, E	E	E
68526-93-2	Nonene, HOF, low-boiling	C10	C9	A, E	E	E
68526-90-9	Nonene, HOF, high-boiling	C10-C11	-	RA	RA	RA
68516-18-7	Decene, HOF	C11	C10	A, O	E	E
68527-06-0	Dodecene, HOF	C13	C12	O	A	RA
68526-92-1	Dodecene, HOF, low-boiling	C13	C10-C12	O	A	RA
68526-91-0	Dodecene, HOF, high-boiling	C13-C14	-	RA	RA	RA

A **Measured data for the alcohol** (study is reliable without restriction; robust summary available).
O **Measured data for the olefin** (study is reliable without restriction; robust summary available).
E Modeled data from ECOSAR for a fish, invertebrate, and/or alga, for the alcohol and/or olefin component.
RA Read Across

Table 6. Olefin Hydroformylation Products Data Matrix for Aquatic Toxicity, Measured and Modeled Component Data Associated with each Product

Olefin Hydroformylation Product		Fish Acute Toxicity 96-hour	Invertebrate Acute Toxicity 48-hour	Alga Toxicity 96-hour
CAS #	Product Name			
68527-03-7	Pentene, HOF			
	C6 Alcohol	**97.7 mg/L****	137 mg/L*	73.2 mg/L*
	C5 Olefin	12.5 mg/L*	14.0 mg/L*	9.1 mg/L*
68938-02-2	Pentene, HOF, low-boiling			
	C6 Alcohol	**97.7 mg/L**	137 mg/L*	73.2 mg/L*
	C5 Olefin	12.5 mg/L*	14.0 mg/L*	9.1 mg/L*
70955-11-2	Hexene, HOF			
	C7 Alcohol	**34.5 mg/L**	**63 mg/L**	30.7 mg/L*
	C6 Olefin	**6.6 mg/L**	6.0 mg/L*	4.0 mg/L*
70955-03-2	Hexene, HOF, low-boiling			
	C7 Alcohol	**34.5 mg/L**	**63 mg/L**	30.7 mg/L*
	C6 Olefin	**6.6 mg/L**	6.0 mg/L*	4.0 mg/L*
68526-80-7	Alcohols, C6 and C8 iso, distillation residues			
	C6, C8 Alcohol	**RA**	RA	RA
	-	-	-	-
70955-04-3	Hexene, HOF, High-boiling			
	C7-C8 Alcohol	RA	RA	RA
	-	-	-	-
68527-04-8	Heptene, HOF			
	C8 Alcohol	**14.0 mg/L**	**31.8 mg/L**	12.4 mg/L*
	C7 Olefin	2.1 mg/L*	2.5 mg/L*	1.7 mg/L*
68526-96-5	Heptene, HOF, low-boiling			
	C8 Alcohol	**14.0 mg/L**	**31.8 mg/L**	12.4 mg/L*
	C7 Olefin	2.1 mg/L*	2.5 mg/L*	1.7 mg/L*
68526-88-5	Heptene, HOF, high-boiling			
	C8-C9 Alcohol	RA	RA	RA
	-	-	-	-
68527-05-9	Octene, HOF			
	C9 Alcohol	**10.1 mg/L**	**4.9 mg/L**	**8.5 mg/L**
	C8 Olefin	**0.9 mg/L**	1.0 mg/L*	0.7 mg/L*
68938-03-4	Octene, HOF, low-boiling			
	C9 Alcohol	**10.1 mg/L**	**4.9 mg/L**	**8.5 mg/L**
	C8 Olefin	**0.9 mg/L**	1.0 mg/L*	0.7 mg/L*
68526-89-6	Octene, HOF, high-boiling			
	C9-C10 Alcohol	RA	RA	RA
	-	-	-	-
68938-04-5	Nonene, HOF			
	C10 Alcohol	**3.1 mg/L**	3.0 mg/L*	2.0 mg/L*
	C9 Olefin	0.32 mg/L*	0.41 mg/L*	0.30 mg/L*
68526-93-2	Nonene, HOF, low-boiling			
	C10 Alcohol	**3.1 mg/L**	3.0 mg/L*	2.0 mg/L*
	C9 Olefin	0.32 mg/L*	0.41 mg/L*	0.30 mg/L*

Table 6. Continued

Olefin Hydroformylation Product		Fish Acute Toxicity 96-hour	Invertebrate Acute Toxicity 48-hour	Alga Toxicity 96-hour
CAS #	**Product Name**			
68526-90-9	**Nonene, HOF, high-boiling**			
	C10-C11 Alcohol	RA	RA	RA
	-	-	-	-
68516-18-7	**Decene, HOF**			
	C11 Alcohol	**1.8 mg/L**	1.2 mg/L*	0.82 mg/L*
	C10 Olefin	**0.12 mg/L**	0.16 mg/L*	0.12 mg/L*
68527-06-0	**Dodecene, HOF**			
	C13 Alcohol	**0.42 mg/L**	**0.71 mg/L**	0.13 mg/L*
	C12 Olefin	RA	RA	RA
68526-92-1	**Dodecene, HOF, low-boiling**			
	C13 Alcohol	**0.42 mg/L**	**0.71 mg/L**	0.13 mg/L*
	C10-C12 Olefin	RA	RA	RA
68526-91-0	**Dodecene, HOF, high-boiling**			
	C13-C14 Alcohol	RA	RA	RA
	-	-	-	-

* Modeled data from ECOSAR
** Values in bold represent experimental data
RA Read Across
(†) Read across data from a C13 olefin

Fish Acute Toxicity

Acute experimental toxicity test results are reported for rainbow trout (*Oncorhynchus mykiss*) and fathead minnow (*Pimephales promelas*)(Table 6). Experimental data for the alkyl alcohol components in olefin hydroformylation products show that they have the potential to produce an increasing level of acute toxicity to freshwater fish from approximately 98 to 0.4 mg/L for the lowest to highest molecular weight product. Experimental and modeled data for the olefin components show that they have the potential to produce an increasing level of acute toxicity in a range of 12.5 to 0.12 mg/L.

Based on chemical composition, the olefin hydroformylation products in this category are expected to produce a similar pattern of increasing acute toxicity to freshwater fish with values more closely aligned with their olefinic components. This suggests that the lowest molecular weight product (Pentene, HOF; CAS # 68527-03-7) is expected to produce a fish 96-hour toxicity value of approximately 12.5 mg/L. As the molecular weight of these products increases, acute toxicity values will decrease. The highest molecular weight product (Dodecene, HOF, high-boiling; CAS # 68526-91-0) will be the most acutely toxic with an expected fish 96-hour toxicity value of approximately 0.12 mg/L.

Experimental data for the C5, C7, and C9 olefin components are not available, but results from ECOSAR (1999), an aquatic toxicity computer model, can be used to adequately characterize the aquatic toxicity of these chemical components.

Results of computer modeling for a C6 and C8 olefin are consistent with the experimental data used to characterize the fish acute toxicity of the C6 and C8 olefin

components in this category. This suggests that the ECOSAR model is sufficiently robust to accurately calculate the toxicity of this range of chemicals. Therefore, the modeled values for a C5, C7, and C9 olefin are expected to be consistent with experimental values for these components and they will be used to characterize the range of fish acute toxicity for the olefin components of the Olefin Hydroformylation Products Category. The K_{ow} values used to calculate the fish toxicity for a C5, C6, C7, C8, and C9 olefins were 2.66, 3.15, 3.64, 4.13, and 4.62, respectively. These values were calculated using the EPIWIN (1999) computer model.

Invertebrate Acute Toxicity

Acute experimental toxicity test results are reported for a Daphnid (*Daphnia magna*)(Table 6). Experimental and modeled data for the alkyl alcohol components in olefin hydroformylation products show that they have the potential to produce an increasing level of acute toxicity, to freshwater invertebrates, from approximately 137 to 0.7 mg/L for the lowest to highest molecular weight product. Modeled data for the olefin components show that they have the potential to produce an increasing level of acute toxicity in a range of 14.0 to 0.16 mg/L.

Based on chemical composition, the olefin hydroformylation products in this category are expected to produce a similar pattern of increasing acute toxicity to freshwater fish with values more closely aligned with their olefinic components. This suggests that the lowest molecular weight product (Pentene, HOF; CAS # 68527-03-7) is expected to produce an invertebrate 48-hour toxicity value of approximately 14.0 mg/L. As the molecular weight of these products increases, acute toxicity values will decrease. The highest molecular weight product (Dodecene, HOF, high-boiling; CAS # 68526-91-0) will be the most acutely toxic with an expected invertebrate 48-hour toxicity value of approximately 0.16 mg/L.

Experimental data for the C6 alcohol and C5, C6, C7, C8, C9, and C10 olefin components are not available, but results from ECOSAR (1999), an aquatic toxicity computer model, can be used to adequately characterize the aquatic toxicity of these components. Comparative fish acute toxicity data agree well between measured and calculated toxicity values, which suggests that this model can develop reliable toxicity data for invertebrates.

Results of computer modeling for a C7 and C8 alcohol are consistent with the experimental data used to characterize the toxicity of the C7 and C8 alcohol components in this category. As stated previously, results of computer modeling with C6 and C8 olefins are consistent when compared to experimental values for acute toxicity to fish. This suggests that the ECOSAR model is sufficiently robust to accurately calculate the toxicity of this range of chemical components, both alcohol and olefin, to freshwater invertebrates. Therefore, the modeled value for a C6 alcohol is expected to be consistent with an experimental value for a C6 alcohol in this category. Additionally, the modeled values for a C5, C6, C7, C8, C9, and C10 olefin are expected to be consistent with experimental values for the olefin components in this category. These values will be used to characterize the range of acute toxicity to invertebrates for the Olefin Hydroformylation Products Category. The K_{ow} values used to calculate the

toxicity for the a C6, C7, and C8 alcohol were 1.75, 2.24, and 2.73, respectively. The K_{ow} values used to calculate the toxicity for the C5 through C10 olefins were 2.66, 3.15, 3.64, 4.13, 4.62, and 5.12, respectively. These values were calculated using the EPIWIN (1999) computer model.

Alga Toxicity

An experimental toxicity test result is reported for the freshwater alga (*Scenendesmus quadricauda*)(Table 6) and used as read across data to the C9 alcohol component in this category). This result shows that the C9 alcohol component has the potential to cause acute toxicity (based upon cell growth) at a concentration of approximately 8.5 mg/L. However, this study is not sufficient to adequately characterize the alga toxicity of all the alcohol components in this category. Also, there are no data available for the olefin components in this category.

Although experimental data for most alcohol and all olefin components are not available, results from ECOSAR can be used to adequately characterize the aquatic toxicity of these components. Modeled data for the component chemicals (alcohol and olefin) show that these components have the potential to produce an increasing level of acute toxicity to a freshwater alga in a range of 73.2 to 0.12 mg/L. Based on chemical composition, the olefin hydroformylation products in this category are expected to produce a similar pattern of increasing acute toxicity to an alga with values more closely aligned with their olefinic components.

The ECOSAR model is sufficiently robust to accurately calculate the toxicity of this range of chemical components based on the measured and calculated values for the C9 alcohol and the comparable fish and invertebrate data (the measured alga value was 8.5 mg/L, while the calculated value was 6.0 mg/L). Therefore, the modeled values for the C6 through C13 alcohol and C5 through C12 olefin components are expected to be consistent with experimental values for their respective components in this category. These values will be used to characterize the range of acute toxicity to a freshwater alga for the Olefin Hydroformylation Products Category. The K_{ow} values used to calculate the toxicity for the C6 through C13 alcohol were 1.82, 2.31, 2.81, 3.30, 3.79, 4.28, and 5.26, respectively. The K_{ow} values used to calculate the toxicity for the C5 through C10 olefins were 2.66, 3.15, 3.64, 4.13, 4.62, and 5.12, respectively. These values were calculated using the EPIWIN (1999) computer model.

Experimental data for toxicity to an alga will be developed for a C6 and C13 alcohol as part of the HPV test plan for the Alkyl Alcohols C6-C13 Category (EMCCb). Experimental data for a C6 internal olefin (60-74% branched) will also be developed for the C6, C7, C8, C9, and C12 Internal Olefins and C16 and C18 Alpha Olefins Category (ACC, 2001). These data will be made available through the HPV Chemical Challenge Program and will be used as read across to fill the measured data gaps and to further support the expected aquatic toxicity of this category.

E. Environmental Fate

Biodegradation data are available for three alcohol and three higher olefin components of the Olefin Hydroformylation Products Category. They show that the alcohol components of these products have the potential to biodegrade to a great extent with a standard 28-day test duration. Conversely, the olefinic components show the potential to biodegrade, but to a lesser extent within a standard 28-day test duration. These results suggest that the products in this category will not persist in the environment.

Biodegradation

Olefin Hydroformylation Product		Component		Read Across Biodegradation Strategy	Percent Biodegradation 28-days
CAS #	Product Name	Alcohol	Olefin		
68527-03-7	Pentene, HOF	C6	C5	RA	RA
68938-02-3	Pentene, HOF, low-boiling	C6	C5	RA	RA
70955-11-2	Hexene, HOF	C7	C6	RA	RA
70955-03-2	Hexene, HOF, low-boiling	C7	C6	RA	RA
68526-80-7	Alcohols, C6 and C8 iso, distillation residues	C6, C8	-	RA	RA
70955-04-3	Hexene, HOF, high-boiling	C7-C8	-	RA	RA
68527-04-8	Heptene, HOF	C8	C7	A, O	**82%, 29%**
68526-96-5	Heptene, HOF, low-boiling	C8	C7	A, O	**82%, 29%**
68526-88-5	Heptene, HOF, high-boiling	C8-C9	-	RA	RA
68527-05-9	Octene, HOF	C9	C8	RA	RA
68938-03-4	Octene, HOF, low-boiling	C9	C8	RA	RA
68526-89-6	Octene, HOF, high-boiling	C9-C10	-	RA	RA
68938-04-5	Nonene, HOF	C10	C9	A, O	**71%, 21%**
68526-93-2	Nonene, HOF, low-boiling	C10	C9	A, O	**71%, 21%**
68526-90-9	Nonene, HOF, high-boiling	C10-C11	-	RA	RA
68516-18-7	Decene, HOF	C11	C10	RA	RA
68527-06-0	Dodecene, HOF	C13	C12	A	**58%**
68526-92-1	Dodecene, HOF, low-boiling	C13	C10-C12	A, O	**58%, 8%†**
68526-91-0	Dodecene, HOF, high-boiling	C13-C14	-	RA	RA

A **Measured data for the alcohol** (study is reliable without restriction; robust summary available).
O **Measured data for the olefin** (study is reliable without restriction; robust summary available).
RA Read Across (†) Read across data from a C13 olefin.

C8 and C10 alcohols have been shown to biodegrade rapidly using a 28-day standard biodegradation test procedure. In comparison, C13 alcohols biodegrade to slightly

lower but significant extent, which suggests that although they are not expected to degrade at rates equivalent to the lighter alcohol components, they will not persist in the environment. Conversely, the olefinic components show the potential to biodegrade, but to a lesser extent within a standard 28-day test duration.

Upon review of the available information, sufficient quality data were identified to accurately characterize the biodegradability of the products in this category. Based on the component data, the olefin hydroformylation products are expected to exhibit a range of biodegradation (28 days) from approximately 50 to 30% for the low to high molecular weight products, respectively. These data were developed using non acclimated inocula obtained from wastewater treatment plants. The tests used closed systems, which is recommended when assessing the biodegradability of materials with a potential to volatilize like those in this category. The test systems were continuously stirred, which is also recommended when evaluating mixtures containing several chemicals, some of which may have minimal water-solubility.

In addition, biodegradation data for a selected C5 olefin will become available from testing proposed by the American Chemistry Council, Olefins Panel in their C5 Non-Cyclics Test Plan. This data will be used to characterize the potential biodegradability of the lower molecular weight olefin hydroformylation products.

Photodegradation – Photolysis (Direct)

Direct photochemical degradation occurs through the absorbance of solar radiation by a chemical substance. If the absorbed energy is high enough, then the resultant excited state of the chemical may undergo a transformation. Simple chemical structures can be examined to determine whether a chemical has the potential for direct photolysis in water. First order reaction rates can be calculated for some chemicals that have a potential for direct photolysis using the procedures of Zepp and Cline (Zepp, 1977).

UV light absorption of the chemical components in this category will be evaluated to identify those having the potential to degrade in solution. For those compounds with a potential for direct photolysis in water, first order reaction rates will be calculated.

Photodegradation – Atmospheric Oxidation (Indirect)

Photodegradation can be measured (US EPA, 1999a) (EPA identifies OECD test guideline 113 as a test method) or estimated using models accepted by the EPA (US EPA, 1999b). An estimation method accepted by the EPA includes the calculation of atmospheric oxidation potential (AOP). Atmospheric oxidation as a result of hydroxyl radical attack is not direct photochemical degradation, but rather indirect degradation. AOPs can be calculated using a computer model. Chemicals, such as those in the Olefin Hydroformylation Products Category, have the potential to volatilize to air.

In air, chemicals can undergo reaction with photosensitized oxygen in the form of hydroxyl radicals (OH-). The computer program AOPWIN (atmospheric oxidation program for Microsoft Windows) (EPIWIN, 1999) is used by OPPTS (Office of Pollution Prevention and Toxic Substances). This program calculates a chemical half-life based

on an overall OH- reaction rate constant, a 12-hr day, and a given OH- concentration. This calculation will be performed for the representative chemical components in the Olefin Hydroformylation Products Category.

Stability in Water (Hydrolysis)

Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Neely, 1985).

Stability in water can be measured (US EPA, 1999a) (EPA identifies OECD test guideline 111 as a test method) or estimated using models accepted by the EPA (US EPA, 1999b). However, all of the chemical structures included in the Olefin Hydroformylation Products Category are mixtures of iso-alcohols and higher olefins. As such they are not expected to hydrolyze at a measurable rate. A technical document will be prepared that discusses the potential hydrolysis rates of these substances, the nature of the chemical bonds present, and the potential reactivity of this class of chemicals with water.

Chemical Transport and Distribution in the Environment (Fugacity Modeling)

Fugacity based multimedia modeling can provide basic information on the relative distribution of chemicals between selected environmental compartments (i.e., air, soil, sediment, suspended sediment, water, biota). The US EPA has acknowledged that computer modeling techniques are an appropriate approach to estimating chemical partitioning (fugacity is a calculated endpoint and is not measured). A widely used fugacity model is the EQC (Equilibrium Criterion) model (Mackay, 1996). EPA cites the use of this model in its document titled *Determining the Adequacy of Existing Data* (US EPA, 1999a), which was prepared as guidance for the HPV Program.

In its document, EPA states that it accepts Level I fugacity data as an estimate of chemical distribution values. The input data required to run a Level I model include basic physicochemical parameters; distribution is calculated as percent of chemical partitioned to 6 compartments (air, soil, water, suspended sediment, sediment, biota) within a unit world. Level I data are basic partitioning data that allow for comparisons between chemicals and indicate the compartment(s) to which a chemical is likely to partition.

The EQC Level I is a steady state, equilibrium model that utilizes the input of basic chemical properties including molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment. This model will be used to calculate distribution values for representative chemical components identified in products in this category. A computer model, EPIWIN – version 3.04 (EPIWIN, 1999), will be used to calculate the properties needed to run the Level I EQC model.

IV. TEST PLAN SUMMARY

ExxonMobil Chemical believes that the olefin hydroformylation products should be further examined in the following manner:

- Calculate physicochemical data as described in the EPA document titled, *The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program* for selected chemical components in this category. Provide measured data for selected products where readily available.
- Prepare a technical discussion on the potential of olefin hydroformylation products in this category to photodegrade. Calculate AOP values for selected chemical components of products in this category.
- Prepare a technical discussion on the potential of olefin hydroformylation products in this category to hydrolyze.
- Calculate fugacity data for selected chemical components of olefin hydroformylation products in this category.
- Forthcoming data on the higher olefins will be used to support read across to Olefin Hydroformylation Products for subchronic, developmental, and reproductive toxicity endpoints.

The data presented in this test plan are adequate to characterize selected HPV Program endpoints for olefin hydroformylation products. Since the olefin hydroformylation products are composed of alkyl alcohols and olefins, the available toxicity data for the alkyl alcohols and olefins are ideal for evaluating the toxicity of the olefin hydroformylation products. ExxonMobil Chemical Company believes that olefin hydroformylation products do not require further testing based on:

- Adequate toxicity data on alkyl alcohols and olefins.
- A consistent pattern of toxicity for alkyl alcohols and olefins.

ExxonMobil Chemical Company believes the thorough evaluation of the strategic anchor studies and the overall robustness of the data set for the olefin hydroformylation products category complies with the objectives of the HPV Program.

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